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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/306,662	05/05/1999	MARK K. MALMROS	PRO-SE	3760

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EXAMINER	
RAWLINGS, STEPHEN L	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/306,662	MALMROS ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 October 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *08 October 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See attached Note of Explanation.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attached Note of Explanation*.

6.☒ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1, 5, 7-11, and 20*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *See attached Note of Explanation*

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Note of Explanation

1. The amendment filed October 8, 2004 is acknowledged and has been entered. Claim 1 has been amended.

2. The declaration under 37 CFR § 1.132 by Michael R. Hamblin, Ph.D. is acknowledged; however, the merit of the declaration has not been considered because it is not directed solely to issue that were raised by the Examiner in the Final Office action. See MPEP § 716.01.

3. The amendment filed October 8, 2004 to claim 1 has obviated the following grounds of objection or rejection set forth the previous Office action mailed June 8, 2004:

(a) The ground of objection of claim 1 set forth in section 5 (page 2).

(b) The grounds of rejection of claims 1, 5, 7-11, and 20 under 35 USC § 112, second paragraph, set forth in section 9, paragraphs 5-7 (pages 5-7).

4. The following grounds of rejection set forth the previous Office action mailed June 8, 2004 have been maintained:

(a) The ground of rejection of claims 1, 5, 7-11, and 20 under 35 USC § 112, first paragraph, set forth in section 7.

(b) The ground of rejection of claims 1, 5, 7-11, and 20 under 35 USC § 112, second paragraph, set forth in section 9, paragraph 4.

(c) The ground of rejection of claims 1, 5, 7-11, and 20 under 35 USC § 102(e) set forth in section 11.

(d) The ground of rejection of claims 1, 5, 7-11, and 20 under 35 USC § 103(a) set forth in section 13.

5. The merit of Applicant's amendment and their accompanying arguments have been carefully considered but not found persuasive to overcome rejection of claims 1, 5,

7-11, and 20 under 35 USC § 112, first paragraph, set forth in section 7 for the following reasons:

Most, if not all of Applicant's arguments at pages 4-6 of the amendment filed October 8, 2004rely upon evidence set forth in the declaration under 37 CFR § 1.132 by Michael R. Hamblin, Ph.D.; however, the merit of the declaration has not been considered.

Nevertheless, it is noted that by reference to the declaration, Applicant has asserted that written support for the terminology of claim 1 appears in the specification at page 8, lines 9-16, and page 22, lines 1-5. The reason that these particular disclosures fail to provide proper and adequate written support for the terminology has been set forth in section 7 of the previous Office action.

By further reference to the declaration, Applicant has also asserted that written support for the terminology of claim 1 appears in the specification at page 8, line 29, to page 9, line 7. However, the Examiner does not find that this disclosure provides written support for the recitation of the terms "the degree of the metachromatic shift of the dye from the reflected light spectrum of the stained tissue or cells" and "the degree of the metachromatic shift of the dye from a library". Notably, the disclosure to which Applicant has referred teaches that the spectroscopic analysis need not be performed using a metachromatic dye (page 8, line 30, through page 9, line 1), so the disclosure does not address the claimed invention with particularity. Furthermore, the disclosure teaches only that the correlation between the measured spectra of stained cells displaying various stages of metaplasia following their illumination and their stage of metaplasia is accomplished by comparing the reflectance spectrum of the stained tissue or lesion with a library or composite of spectra from lesions that have been similarly stained and subsequently diagnosed by conventional or classical histochemical methods. It fails to teach or suggest that such a correlation can be accomplished by comparing "the **degree of the metachromatic shift** of the dye from the reflected light spectrum of the stained tissue or cells" with **the degree of the metachromatic shift** of the dye from a library" (emboldened for emphasis). Accordingly, the Examiner

disagrees with Applicant's assertions that specification, including the claims, as originally filed, provides written support for the language recited in the present claims.

6. The merit of Applicant's amendment and their accompanying arguments have been carefully considered but not found persuasive to overcome rejection of claims 1, 5, 7-11, and 20 under 35 USC § 112, second paragraph, set forth in section 9, paragraph 4, for the following reasons:

Most, if not all of Applicant's arguments at pages 6 and 7 of the amendment filed October 8, 2004 rely upon evidence set forth in the declaration under 37 CFR § 1.132 by Michael R. Hamblin, Ph.D.; however, the merit of the declaration has not been considered.

Nevertheless, it is noted that by reference to the declaration, Applicant has asserted that the specification defines the term "the degree of the metachromatic shift" at page 21, line 29, through page 22, line 5. To the contrary, however, the disclosure to which Applicant has referred does not explicitly define the term, nor does the passage recite the term. The disclosure teaches that the software analysis of the reflectance spectra may compare the metachromatic shift of the stain between two or more specific wavelengths by correlation; but it does not teach measuring the degree of the metachromatic shift. *Arguendo*, if it were to be understood that the metachromatic shift is a *change* in wavelength measured in nanometers, as Applicant has asserted at page 7 of the amendment, then it still unclear what feature of the spectra is measured at two different wavelengths and still unclear what value constitutes the degree of the metachromatic shift. Furthermore, given the proffered definition, it is unclear how one can measure the "degree" (extent) of such a shift (i.e., a change in wavelength measured in nanometers) between more than two wavelengths, as disclosed at page 22, lines 1-3, of the specification, since a change (i.e., a difference) can only be measured between two points, not more than two. Accordingly, the Examiner disagrees with Applicant's assertions that the metes and bounds of the subject matter that Applicant regards as the invention are clearly and particularly delineated by the instant claims.

7. The merit of Applicant's amendment and their accompanying arguments have been carefully considered but not found persuasive to overcome rejection of claims 1, 5, 7-11, and 20 under 35 USC § 102(e) set forth in section 11 for the following reasons:

Most, if not all of Applicant's arguments at pages 10-20 of the amendment filed October 8, 2004 rely upon evidence set forth in the declaration under 37 CFR § 1.132 by Michael R. Hamblin, Ph.D.; however, the merit of the declaration has not been considered.

Nevertheless, it is noted that by reference to the declaration, Applicant has asserted that the prior art fails to anticipate the claimed invention. The Examiner disagrees.

At page 15 of the amendment, Applicant has again argued that the prior art does not teach methods for diagnosing cancer, apart from methods that rely upon detecting spatial organization or distribution of cellular contents, or quantifying such cellular contents. This argument has been adequately addressed in the previous Office action at pages 7-12.

At pages 16 and 17, Applicant has asserted that the Examiner has incorrectly defined the term "metachromasia" at page 8 of the previous Office action. However, contrary to Applicant's assertion, the term is correctly defined as evidenced, for example, by the On-line Medical Dictionary (published at the Dept. of Medical Oncology, University of Newcastle upon Tyne © Copyright 1997-2004 - The CancerWEB Project), which is available on the Internet at http://cancerweb.ncl.ac.uk/omd/. The On-line Medical Dictionary defines the term as "[t]he situation where a stain when applied to cells or tissues gives a colour different from that of the stain solution". Accordingly, contrary to Applicant's assertion at page 17 of the amendment, metachromasia is an inherent property of the dye, rather than "a property of the interaction between the dye and the tissue or cell that is being stained". Notably, not all dyes are metachomatic; thus, it follows that metachromasia is a property of the dye.

At page 17 of the amendment, Applicant has remarked that the prior art does expressly recite the term "metachromatic shift", but the prior art teaches metachromatic

dyes are used to differentially stain cells or tissues *in situ* to enable diagnosis following a comparison of the reflected light spectrum of stained cells or tissues with a library of spectra and correlation of reflected light spectra with a pathology. Again, there is no manipulative difference between the steps practiced in performing the claimed invention and those practiced in performing the prior art's disclosed methods for diagnosing cancer. The methods of the prior art differentiate cancerous tissue and normal tissue on the basis of differences or similarities that are observed in the transmission spectra of a dye after staining a sample containing suspected cancerous cells and a library of tissues or cells that have been previously characterized as either cancerous or not. Therefore, in practicing the method of the prior art, the artisan necessarily determined the metachromatic shift of the dye that was used to stain the tissues or cells.

Also at page 17, Applicant has again argued that the prior art is broad and includes a number of applications of the disclosed device and methodology without suggesting the device is useable in diagnosing cancer. This argument has been sufficiently addressed in the previous Office action.

Furthermore, Applicant has argued that the prior art teaches a stain composition comprising more than one dye, which would result in the presence of multiple colors, thereby interfering with an examination of the change in color of the single metachromatic dye. This argument is not persuasive, since the prior art merely exemplifies one application of the disclosed device and methodology that utilizes such a combination of dyes; but moreover, as Applicant has noted, the instant specification teaches at page 22, for example, that combinations of dyes can be used in practicing the claimed invention. Notably, also, the original claims recited the use of a combination of dyes, including at least one metachromatic dye.

While Applicant has reiterated other arguments in the amendment, it is believed that these arguments have been adequately addressed in the previous Office action.

8. The merit of Applicant's amendment and their accompanying arguments have been carefully considered but not found persuasive to overcome rejection of claims 1, 5, 7-11, and 20 under 35 USC § 103(a) set forth in section 13 for the following reasons:

Applicant's arguments at pages 10-20 of the amendment filed October 8, 2004 rely upon evidence set forth in the declaration under 37 CFR § 1.132 by Michael R. Hamblin, Ph.D.; however, the merit of the declaration has not been considered.

Nevertheless, it is noted that by reference to the declaration, Applicant has asserted that the prior art fails to suggest the claimed invention. The Examiner disagrees.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
January 25, 2005

LARRY R. HELMS, PH.D
PRIMARY EXAMINER